Docket No. 70207/48,913-C

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:

Pcter C. Meltzer, et al.

SERIAL NO.

09/975,586

examiner: C. Aulakh

OFFICIAL

filed:

October 11, 2002

GROUP:

1625

VIIIVIAL

FOR:

**BOAT TROPANES** 

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Commissioner for Patents P.O. Box 1450 Arlington, VA 22313-1450

SEP 0 9 2003

Sir:

## Ccrtificate of Mailing

I hereby certify that this correspondence is, on the date shown below, being deposited
with the United States Postal Service with sufficient postage as first class mail in an
cnvelope addressed to Commissioner of Patents, P.O. Box 1450, Arlington, VA
22313-14500th
Daise 1 L. Rose
Denise A. Rose

## DECLARATION UNDER 37 C.F.R. 1.132

- I, Peter C. Meltzer, declare that:
- 1. I hold a Ph.D. in Organic Chemistry from the University of the Wiwatersrand,
- S. Africa. After obtaining my PhD, I was awarded a Post-doctoral fellowship at Massachusetts Institute of Technology.
- 2. I am one of the inventors of the above-identified U.S. Patent Application Serial Number 09/975,586.

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- 3. I have over 13 years experience in research and development of synthetic tropanes and their use in connection with diagnosis and treatment of conditions involving the dopamine transporter. My current curriculum vitae is attached as Appendix A.
- 4. I understand that the Examiner has rejected claims 22-27 over Clarke U.S. Patent No. 3,813,404. The examiner states that

The disclosed compounds of Clarke (see examples 1-14 and claims 1-8) differ from the instant compounds in having the instant R2 group as a 3-beta isomer instead of a 3-alpha isomer. However, Clark teaches that any stereochemical arrangement of the nucleus and substituent groups is contemplated (see col. 1, lines 48-50). Therefore, it would have been obvious to one skilled in the art to prepare the instant compounds having R2 group as 3-alpha isomer by modifying 3-beta isomer since Clarke [sic] teaches this interchangeability for the substituents as mentioned above.

- 5. In my opinion, the examiner's conclusion that it would have been obvious "to prepare the instant compounds having R2 group as 3-alpha isomer by modifying 3-beta isomer" of Clarke is erroneous. Based on my knowledge and experience in the art, the presently claimed 3-alpha compounds cannot be prepared by using the Grignard reactions used by Clarke.
- 6. Initially, it was not obvious to us that we should try to prepare the 3-alpha boat tropanes. Only after we had prepared the boat tropanes through a new synthesis route did we unexpectedly discover that they were more DAT selective than the corresponding chair (3-beta) compounds. We were quite surprised at the potency and selectivity of the 3-alpha tropanes.

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I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing therein.

Date: 7/22/03

Peter C. Meltzer

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